

Amendments to the Claims

This listing of the claims will replace all prior versions, and listings, of claims in this application.

Listing of Claims

1-24. **Canceled.**

25. **(New)** A method of screening for compounds which reduce antibiotic resistance in a highly antibiotic resistant microbe comprising an AcrAB or AcrAB-like efflux pump, wherein the microbe comprises at least two of the following traits: i) at least one chromosomal mutation in a gene encoding an antibiotic target that renders the microbe resistant to one or more antibiotics; ii) a second mutation (to the same gene or a different gene than in (i)) that further increases antibiotic resistance, and iii) increased expression of at least one efflux pump, comprising: contacting the microbe with a test compound and measuring the effect of the test compound on the activity of the AcrAB or AcrAB-like efflux pump, wherein compounds which inhibit the activity of the AcrAB or AcrAB-like efflux pump are identified as compounds which reduce antibiotic resistance in the microbe.

26. **(New)** The method of claim 25, wherein the microbe comprises all three of the traits.

27. **(New)** The method of claim 25, wherein the microbe is highly resistant to fluoroquinolones.

28. **(New)** The method of claim 25, wherein the at least one chromosomal mutation is present in a gene selected from the group consisting of: gyrase and topoisomerase.

29. **(New)** The method of claim 25, wherein the microbe is a Gram negative bacterium.

30. (New) The method of claim 25, wherein the microbe further comprises functional porin channels.

31. (New) The method of claim 25, wherein the microbe is contacted with test compounds selected from a library of test compounds.

32. (New) The method of claim 25, wherein the activity of the AcrAB or AcrAB-like efflux pump is determined by measuring efflux of an indicator compound which is a substrate of the efflux pump.

33. (New) The method of claim 25, wherein the activity of the AcrAB or AcrAB-like efflux pump is determined by measuring growth of the microbe in an antibiotic.

34. (New) The method of claim 25, wherein the efflux pump is AcrAB.

35. (New) A method of screening for compounds which specifically inhibit the activity of an AcrAB or AcrAB-like efflux pump comprising:

i) contacting a microbe comprising an AcrAB or AcrAB-like efflux and a non-AcrAB or non-AcrAB-like efflux pump and at least two of the following traits: i) at least one chromosomal mutation in a gene encoding a antibiotic target that renders the microbe resistant to one or more antibiotics; ii) a second mutation (to the same gene or a different gene than in (i)) that further increases antibiotic resistance, and iii) increased expression of at least one efflux pump, with a test compound and an indicator compound;

ii) testing the ability of the test compound to inhibit the activity of the AcrAB or AcrAB-like efflux pump;

iii) testing the ability of the test compound to inhibit the activity of the non-AcrAB or non-AcrAB efflux pump;

iv) and identifying compounds which inhibit the activity of the AcrAB or AcrAB-like efflux pump relative to the non-AcrAB or non-AcrAB-like efflux pump to thereby identify compounds which specifically inhibit the activity of the AcrAB or AcrAB-like efflux pump.

36. (New) The method of claim 35, wherein the microbe is highly antibiotic resistant.

37. (New) The method of claim 35, wherein the microbe is highly resistant to fluoroquinolones.

38. (New) The method of claim 35, wherein the at least one mutation is present in a gene selected from the group consisting of: gyrase and topoisomerase.

39. (New) The method of claim 35, wherein the microbe is a Gram negative bacterium.

40. (New) The method of claim 35, wherein the microbe further comprises functional porin channels.

41. (New) The method of claim 35, wherein the microbe is contacted with test compounds selected from a library of test compounds.

42. (New) The method of claim 35, wherein the activity of the AcrAB or AcrAB-like efflux pump is determined by measuring efflux of an indicator compound which is a substrate of the efflux pump.

43. (New) The method of claim 35, wherein growth of the microbe in an antibiotic is measured.

44. (New) The method of claim 35, wherein the efflux pump is AcrAB.

45. (New) A method of treating an infection in a subject caused by a microbe comprising an AcrAB or AcrAB-like efflux pump and at least two of the following traits: i) at least one chromosomal mutation in a gene encoding a antibiotic target that renders the microbe resistant to one or more antibiotics; ii) a second mutation (to the same gene or a different gene than in (i)) that further increases antibiotic resistance, and iii) increased expression of at least one

efflux pump, comprising: contacting the microbe with an antibiotic to which the microbe is resistant and an inhibitor of an acrAB or acrAB-like efflux pump such that the infection in the subject is treated.

46. (New) The method of claim 45, wherein the subject is treated prophylactically.
47. (New) The method of claim 45, wherein the subject is treated therapeutically.
48. (New) The method of claim 45, wherein the microbe is highly resistant to fluoroquinolones.
49. (New) The method of claim 45, wherein the at least one mutation is present in a gene selected from the group consisting of: gyrase and topoisomerase.
50. (New) The method of claim 45, wherein the microbe is a Gram negative bacterium.
51. (New) The method of claim 45, wherein the microbe further comprises functional porin channels.